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Det C1

1. (Twice amended) A method of detecting a splicing defect in a human dihydropyrimidine dehydrogenase gene, comprising determining whether the residue of a human genomic DNA encoding the human dihydropyrimidine dehydrogenase gene at the position indicated as nucleotide 434 of SEQ ID NO: 1 is a G residue or determining whether the residue at the position indicated as nucleotide 434 of SEQ ID NO: 1 is an A residue, wherein said gene the substitution of the G residue with an A residue at said position causes a splicing defect in the human dihydropyrimidine dehydrogenase gene.

2. (Twice amended) The method of claim 1, wherein the method comprises the step of amplifying human intronic dihydropyrimidine dehydrogenase genomic DNA to detect therein a G residue or an A residue at the position indicated as nucleotide 434 of SEQ ID NO: 1.

3. (Twice amended) The method of claim 2, wherein the method comprises amplifying the genomic DNA with a primer complementary to a subregion of the human dihydropyrimidine dehydrogenase genomic nucleotide sequence of SEQ ID NO: 1.

Det C2

4. (Twice amended) The method of claim 2, wherein the detecting is by digestion of the amplified DNA with a restriction endonuclease.

5. (Twice amended) The method of claim 1, wherein the determining is by oligonucleotide array.

Det C3

6. (Twice amended) A method of screening human patients for sensitivity to 5-fluorouracil, comprising isolating a genomic DNA from the patient and determining whether a G residue is the residue of the DNA at the position indicated as nucleotide 434 of SEQ ID NO: 1.

7. (Twice amended) The method of claim 6, wherein the method comprises the step of amplifying human intronic dihydropyrimidine dehydrogenase genomic DNA from the patient and determining if the residue at the position indicated as nucleotide 434 of SEQ ID NO: 1 is a G residue or determining if the residue at the position indicated as nucleotide 434 of SEQ ID NO: 1 is an A residue.

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8. (Twice amended) The method of claim 7, wherein the method comprises amplifying the genomic DNA with a primer complementary to a subregion of the human dihydropyrimidine dehydrogenase genomic nucleotide sequence of SEQ ID NO: 1.

9. (Twice amended) The method of claim 7, wherein the determining is by digestion of the amplified DNA with a restriction endonuclease.

Pub C4

10. (Twice amended) A composition comprising a PCR primer complementary to a subregion of a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence of SEQ ID NO: 1.

11. (Twice amended) The composition of claim 10, wherein the PCR primer is complementary to a subregion of a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

Concluded

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15. (Twice amended) A kit comprising a container, a first PCR primer complementary to a subregion of DNA 3' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, and a second PCR primer complementary to a subregion of DNA 5' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, wherein at least one of the first or second PCR primers is complementary to a subregion of a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence of SEQ ID NO: 1.

16. (Twice amended) The kit of claim 15, wherein the kit further comprises instructions for detecting a G residue or an A residue in human dihydropyrimidine dehydrogenase genomic DNA at the position indicated as nucleotide 434 of SEQ ID NO: 1.

17. (Twice Amended) The kit of claim 15, wherein the kit further comprises a restriction endonuclease which cleaves a human dihydropyrimidine dehydrogenase genomic

B2 DNA only if the residue at the position indicated as nucleotide 434 of SEQ ID NO: 1 is a G residue.

B3 20. (Amended) The method of claim 2, wherein the method comprises amplifying the genomic DNA with a primer complementary to a subregion of a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

21. (Amended) The method of claim 4, wherein the restriction endonuclease cleaves a Mae II cleavage site.

22. (Amended) The method of claim 8, wherein the method comprises amplifying the genomic DNA with a primer which is complementary to a subregion of a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

23. (Amended) The method of claim 9, wherein the restriction endonuclease cleaves a Mae II cleavage site.

24. (Amended) The kit of claim 15, wherein at least one of the first or second PCR primers is complementary to a subregion of a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

25. (Amended) 25. The kit of claim 17, wherein the restriction endonuclease cleaves a Mae II cleavage site.

26. (Amended) A kit comprising a container, a first PCR primer which is complementary to a subregion of the DNA sequence of SEQ ID NO: 1 which is 3' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of the human dihydropyrimidine dehydrogenase, a second PCR primer which is complementary to a subregion of DNA of SEQ ID NO: 1 5' of a splice site in the human genomic DNA for an exon encoding